REMARKS/ARGUMENTS

After entry of the amendment, claims 1, 5-7 and 31-52 remain pending. Claims 6, 7 and 42 have been amended. Claims 7, 31-34 and 51-52 have been withdrawn, and claims 2-4 have been canceled. Applicants reserve the right to pursue such claims in a continuation or divisional application.

SEQUENCE LISTING

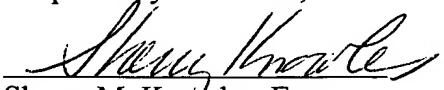
The Examiner has noted that the application does not comply with the requirements of 37 CFR 1.821 through 1.825 for failure to provide sequence identification numbers for all sequences of more than 8 nucleotides or 3 amino acids, particularly regarding page 12 and Seq ID No 19. Applicants enclose herewith a copy of the Notice to Comply with Requirements for Patent Applications containing Nucleotide and/ or Amino Acid Sequence Disclosures, which we believe was filed by the previous Agents for the Applicants (Darby & Darby) on October 28, 2003. This Response included a substitute sequence listing along with the corresponding amendments to the specification to insert the appropriate sequence identifiers. For example, see page 5 of the Response, which amends the specification to insert the appropriate sequence identifiers on page 12; and page 6 of the Response, which inserts Seq ID No 19 in the appropriate text. Applicants believe that the previously submitted Response places the application in compliance with 37 CFR 1.821 through 1.825.

RESTRICTION REQUIREMENT

In response the restriction requirement, Applicants elect Group I, claims 1, 5, 6, 35-50. (Applicants believe that amended claim 42 should now be included as part of the product claim group since it is a further limitation of product claims 41 and 6). Applicants have elected the product claims and reiterate that if the product claims are found allowable, the withdrawn process claims that depend from or otherwise include all of the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04.

It is respectfully believed that this application is ready for examination on the merits. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. The Commissioner is authorized to charge any underpayment of fees and to credit any overpayment to Deposit Account No. 11-0980.

Respectfully submitted,



Sherry M. Knowles, Esq.
Reg. No. 33,052

Date: September 26, 2005

KING & SPALDING LLP
191 Peachtree Street
45th Floor
Atlanta, Georgia 30303-1763
Tel. (404) 572-4600

PTO/SB/22 (08-03)
Approved for use through 7/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket No. (Optional): 02292/000H795-US0

In re Application of	Lechler and Dorling
Application Number: 09/674,462	Filed: May 8, 2001
For:	IMMUNOSUPPRESSION BY BLOCKING T CELL CO-STIMULATION SIGNAL 2(B7/CD28 INTERACTION)
Art Unit: 1644	Examiner: Jessica Roark

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- [X] One month (37 CFR 1.17(a)(1)) — $ 110.00
- [ ] Two months (37 CFR 1.17(a)(2)) — $
- [ ] Three months (37 CFR 1.17(a)(3)) — $
- [ ] Four months (37 CFR 1.17(a)(4)) — $
- [ ] Five months (37 CFR 1.17(a)(5)) — $

[X] Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $ 55.00 .

[X] A check in the amount of the fee is enclosed.

[ ] Payment by credit card. Form PTO-2038 is attached.

[ ] The Director has already been authorized to charge fees in this application to a Deposit Account.

[X] The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 04-0100 .

I have enclosed a duplicate copy of this sheet.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).
- [ ] attorney or agent of record. Registration Number _____
- [X] attorney or agent under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a) 51,658

October 28, 2003
Date

Heather Morehouse Ettinger
Signature

(212) 836-3744
Telephone Number

Heather Morehouse Ettinger, Ph.D.
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below

[ ] Total of 1 forms are submitted.

Express Mail Label No. Dated: _____

PTO/SB/17 (10-02)
Approved for use through 10/31/2002. OMB 0651-0032
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

FEE TRANSMITTAL for FY 2003

Patent fees are subject to annual revision.

[X] Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 55.00

Complete if Known	
Application Number	09/674,462
Filing Date	May 8, 2001
First Named Inventor	Lechler and Dorling
Examiner Name	Jessica Roark
Group Art Unit	1644
Attorney Docket No.	02292/000H795-US0

METHOD OF PAYMENT *(check all that apply)*

[X] Check [ ] Credit Card [ ] Money Order [ ] Other [ ] None

[ ] Deposit Account

Deposit Account Number:

Deposit Account Name:

The Commissioner is hereby authorized to: *(check all that apply)*

[ ] Charge fee(s) indicated below [X] Credit any overpayments

[ ] Charge any additional fee(s) during the pendency of this application

[ ] Charge fee(s) indicated below, **except for the filing fee**

to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	740	2001	370	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	510	2003	255	Plant filing fee	
1004	740	2004	370	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0.00

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

		Extra Claims	Fee from below	Fee Paid
Total Claims	-** =		x =	
Independent Claims	-** =		x =	
Multiple Dependent			=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0.00

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge – late filing fee or oath	
1052	50	2052	25	Surcharge – late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	55.00
1252	400	2252	200	Extension for reply within second month	
1253	920	2253	460	Extension for reply within third month	
1254	1,440	2254	720	Extension for reply within fourth month	
1255	1,960	2255	980	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,280	2453	640	Petition to revive - unintentional	
1501	1,280	2501	640	Utility issue fee (or reissue)	
1502	460	2502	230	Design issue fee	
1503	620	2503	310	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	740	2809	370	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	740	2810	370	For each additional invention to be examined (37CFR 1.129(b))	
1801	740	2801	370	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	
Other fee (specify)					

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 55.00

SUBMITTED BY				Complete *(if applicable)*	
Name (Print/Type)	Heather Morehouse Ettinger, Ph.D.	*Registration No. (Attorney/Agent)*	51,658	*Telephone*	(212) 836-3744
Signature	Heather Morehouse Ettinger			*Date*	October 28, 2003

Atty Docket No.: 02292/000H795-US0

Inventor: Lechler and Dorling

Appln: 09/674,462 **Filed:** May 8, 2001

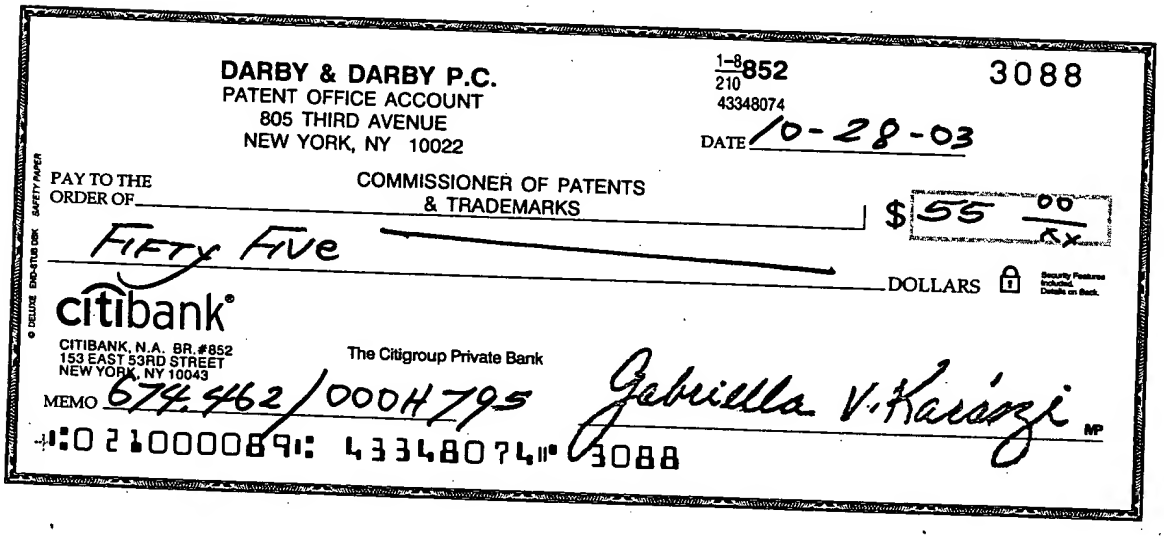
Title: IMMUNOSUPPRESSION BY BLOCKING T CELL CO-STIMULATION SIGNAL 2(B7/CD28 INTERACTION)

Documents:

Response to Office Action (11 pages)
One Month Request for Extension of Time Under 37 CFR 1.136(a) (1 page)
Fee Transmittal (1 page)
Transmittal Form (1 page)
Check in the amount of $55.00 3088
Tab 1 (2 pages)
Substitute Sequence Listing - paper copy (16 pages)
CRF Substitute Sequence Listing (1 diskette)
Certificate of Express Mailing

Via: Express Mail: Airbill No. EV982104097-US

Sender Initials: HME/DBP **Date:** October 28, 2003



DARBY & DARBY P.C.
PATENT OFFICE ACCOUNT
805 THIRD AVENUE
NEW YORK, NY 10022

1-8/210 852
43348074

3088

DATE 10-28-03

PAY TO THE ORDER OF COMMISSIONER OF PATENTS & TRADEMARKS $ 55 00 ex

FIFTY FIVE DOLLARS

citibank
CITIBANK, N.A. BR.#852
153 EAST 53RD STREET
NEW YORK, NY 10043

The Citigroup Private Bank

MEMO 674,462/000H795

Gabriella V. Karaszi MP

⑆021000089⑆ 43348074⑈ 3088

PTO/SB/21 (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

		Application Number	09/674,462
		Filing Date	May 8, 2001
		First Named Inventor	Lechler and Dorling
		Art Unit	1644
		Examiner Name	Jessica Roark
Total Number of Pages in This Submission	1	Attorney Docket Number	02292/000H795-US0

ENCLOSURES (*Check all that apply*)

[X] Fee Transmittal Form	[ ] Drawing(s)	[ ] After Allowance Communication to Group
[X] Fee Attached	[ ] Licensing-related Papers	[ ] Appeal Communication to Board of Appeals and Interferences
[X] Amendment/Reply	[ ] Petition	[ ] Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
[ ] After Final	[ ] Petition to Convert to a Provisional Application	[ ] Proprietary Information
[ ] Affidavits/declaration(s)	[ ] Power of Attorney, Revocation Change of Correspondence Address	[ ] Status Letter
[X] Extension of Time Request	[ ] Terminal Disclaimer	[ ] Other Enclosure(s) (please identify below):
[ ] Express Abandonment Request	[ ] Request for Refund	Substitute Sequence Listing (paper and CRF)
[ ] Information Disclosure Statement	[ ] CD, Number of CD(s) _____	
[ ] Certified Copy of Priority Document(s)		
[ ] Response to Missing Parts/ Incomplete Application	Remarks	
[ ] Response to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	DARBY & DARBY P.C. Heather Morehouse Ettinger, Ph.D. - 51,658
Signature	Heather Morehouse Ettinger
Date	October 28, 2003

Express Mail Label No.	Dated: _____

EXPRESS MAIL CERTIFICATE

Date_____ Label No._____
I hereby certify that, on the date indicated above, this paper or fee was deposited with the U.S. Postal Service & that it was addressed for delivery to the Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 by "Express Mail Post Office to Addressee" service.

_____ _____
Name (Print) Signature

PLEASE CHARGE ANY DEFICIENCY OR CREDIT ANY EXCESS IN THE FEES DUE WITH THIS DOCUMENT TO OUR DEPOSIT ACCOUNT NO. 04-0100

Customer No.: 07278

File No.: 02292/000H795-US0

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Lechler and Dorling

Serial No.: 09/674,462 Group Art Unit: 1644

Filed: May 8, 2001 Examiner: Jessica Roark

Confirmation No.: 8594

For: IMMUNOSUPPRESSION BY BLOCKING T CELL CO-STIMULATION SIGNAL 2 (B7/CD28 INTERACTION)

RESPONSE TO NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATION CONTAINING NUCLEOTIDE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Notice to Comply with Requirements for Patent Application containing Nucleotide and/or amino Acid Sequence Disclosures mailed on July 28, 2003, please consider the following amendments and remarks. Amendments to the specification begin on page 3 of this paper. Remarks begin on page 9 of this paper. Submitted simultaneously herewith is (i) a Petition for ONE (1) MONTH Extension of Time up to and including October 28, 2003 accompanied by the required fee, (ii) paper copy of the Substitute Sequence Listing and CRF of

the substitute sequence listing (1 diskette), (iii) fee transmittal sheet, and (iv) Tab 1 (NCBI printout showing sequence disclosed in Parsons et al. reference).

It is believed that no fee other than the fee for one month's extension of time is due. Should the United States Patent and Trademark Office determine that any other fee(s) is due or that any refund is owed for this application, the Commissioner is hereby authorized and requested to charge the required fee(s) and/or credit the refund(s) owed to our Deposit Account No. 04-0100.

AMENDMENTS TO THE SPECIFICATION

On page 4, beginning at line 19, please amend the specification as follows:

In the context of a pig being the donor organism, the invention provides a protein comprising the amino acid sequence shown in Figure 2 as ~~SEQ ID:1~~ SEQ ID NO: 1, which is CTLA-4 cloned from porcine cells. This is the preferred form of CTLA-4 for use in the invention. The extracellular domain of this protein is also shown in Figure 2.

On page 4, beginning at line 23, please amend the specification or follows:

The invention also provides nucleic acid which encodes protein ~~SEQ ID:1~~ SEQ ID NO: 1 (or fragments thereof). This preferably comprises the nucleotide sequence shown in Figure 3 as ~~SEQ ID:2~~ SEQ ID NO: 2.

On page 10, please amend the table as follows:

Domain	**Human** (SEQ ID NO: 31)	**Bovine** (SEQ ID NO: 32)
Signal peptide	67.6%	86.5%
Extracellular domain	83.8%	84.6%
Transmembrane domain	96.1%	100%
Cytoplasmic domain	100%	100%
Overall	85.2%	89.2%

On page 11, please amend the table as follows:

Domain	Human (SEQ ID NO: 33)	Bovine (SEQ ID NO: 34)
Signal peptide	76%	81.3%
Extracellular domain	85.2%	86.3%
Transmembrane domain	92.3%	96.2%
Cytoplasmic domain	96.5%	97.7%
Overall	86.1%	88.3%

On page 11, beginning at line 2, please amend the specification as follows:

Figure 4 shows the amino acid sequence of the pCTLA4-Ig construct (SEQ ID NO: 3). The underlined sequence shows the flexible linger GGSGGAA (SEQ ID NO: 28), which also denotes the junction between pCTLA4 and the IgG1 domains.

On page 11, beginning at line 13, please amend the specification as follows:

Figure 8 shows the nucleotide sequence of an anti-human CTLA-4 sFv (SEQ ID NO: 4). The inferred protein sequence is shown in **Figure 9** (SEQ ID NO: 5). **Figure 10** (SEQ ID NOS: 6-9) shows the nucleotide sequences of four anti-murine CTLA-4 sFv. The inferred protein sequences are shown in **Figure 11** (SEQ ID NOS: 10-13). The heavy and light chains are linked by a serine-glycine linker as indicated in Figures 9 and 11.[.]

On page 11, beginning at line 21, please amend the specification as follows:

Figure 15 shows (A) the nucleotide sequence (SEQ ID NO: 14) and (B) the amino acid sequence (SEQ ID NO: 15) of human CTLA-4. The start codon is underlined. At position -21, the sequence differs from GenBank sequence L15006, and at position 110 the sequence differs from both L15006 and M74363.

On page 12, beginning at line 1, please amend the specification as follows:

Figure 16 shows the sequence of cloned human CD8α (SEQ ID NO: 16). This differs from the GenBank sequence at positions 231 (T → G), 244 (A → G), 266 (T → C), and 437 (T → C).

On page 12, beginning at line 17, please amend the specification as follows:

Porcine CTLA-4 ("pCTLA4") was cloned from PHA-activated pig T cells. RNA was prepared using standard techniques and pCTLA4 was amplified by PCR using primers:

5' -TTGAAGCTTAGCCATGGCTTGCTCTGGA- 3' (SEQ ID NO: 17) (5' primer)

5' -TAATGAATTCTCAATTGATGGGAATAAAATAAG -3' (SEQ ID NO: 18) (3' primer)

On page 12, beginning at line 25, please amend the specification as follows:

The predicted amino acid sequence of pCTLA4 is shown in figure 2, with a comparison with that of human and cattle. Of significance is the predicted amino acid difference at residue 97, which is important in B7 binding, being part of the conserved hexapeptide motif MYPPPY (SEQ ID NO: 29). In pCTLA4, residue 97 is leucine (giving LYPPPY (SEQ ID NO: 30)), whereas other

species have methionine (although leucine has also been found in bovine CD28 (21)). This important amino acid difference is believed to be of key importance to the advantageous differential binding of pCTLA4 to human and pig B7.

On page 13, line 3, please amend the specification as follows (Please note that the text "**TGCAG**CACCACCGGAGCCACC" has not been added by way of this amendment. This text was underlined in the specification as filed and it should be underlined in the unmarked version of this paragraph.):

The extracellular domain of pCTLA4 was amplified using the 5' primer described above and:

5'-CGGTTC**TGCAG**CACCACCGGAGCCACCATCAGAATCTGGGCATGGTTCTGGAT CAATGAC-3' (SEQ ID NO: 19)

This amplified from position 484, introduced an 18 base-pair segment encoding a linker GGSGGAA (SEQ ID NO: 28) sequence (underlined), and introduced a *Pst*I site (bold) to allow in-frame ligation to the hinge region of human IgG1. The resulting 500bp fragment was sub-cloned into *Hind*III/*Pst*I digested pBluescript-IgG1 containing genomic DNA encoding intronic sequences and the hinge, CH2, CH3 and 3' untranslated exons of human IgG1 between *Pst*I/*Not*I sites. The amino acid sequence of the resulting soluble pCTLA4-Ig is shown in figure 4.

On page 15, beginning at line 7, please amend the specification as follows (Please note that the text "GCGGCCG" and "CTGCAG" has not been added by way of this amendment. This text was underlined in the specification as filed and it should be underlined in the unmarked version of this paragraph.):

The *myc* sequences from pHOOK1 were amplified by PCR using the 5' primer 5'-GAGCTGAAACGGGCGGCCGCAGAAC-3' (SEQ ID NO: 20), which contains a *Not*I site (underlined) and the 3' primer 5'-CTGGCCTGCAGCATTCAGATCC-3' (SEQ ID NO: 21), which introduced a *Pst*I site (underlined). The resulting 113 base pair fragment was sub-cloned into *Not*I/*Pst*I digested pBluescript.

On page 16, beginning at line 7, please amend the specification as follows:

RNA from PHA-activated human T cells was prepared using standard techniques. hCTLA4 was amplified PCR using primers:

5'-TTCAAAGCTTCAGGATCCTGAAAGGTTTTG-3' (SEQ ID NO: 22) introducing a *Hind*III site (5' primer)

5'-TAATGAATTCTCAATTGATGGGAATAAAATAAG-3' (SEQ ID NO: 23) introducing a *EcoR*I site (3' primer)

On page 16, beginning at line 15, please amend the specification as follows (Please note that the text "ACCACCGGAGCCACC" has not been added by way of this amendment. This text was underlined in the specification as filed and it should be underlined in the unmarked version of this paragraph.):

The extracellular domain of hCTLA-4 was amplified using 5' primer described above and:

5'-GATGTAGATATCACAGGCGAAGTCGACACCACCGGAGCCACCAATTACATAA ATCTGGGCTCCGTTGCCTATGCCC-3' (SEQ ID NO: 24)

This amplified from position 457 and included a 15 base segment encoding a flexible GGSGG (SEQ ID NO: 35) amino acid linker (underlined), along with a unique *Sal*I site (highlighted).

The resulting fragment was sub cloned into *Hind*III/*Eco*RI digested pBluescript and sequenced. hCD8 was PCR-amplified from resting T-cells using primers:

5'-TCGCGCCCAAGCTTCGAGCCAAGCAGCGT-3' (SEQ ID NO: 25) introducing a *Hind*III site (5' primer)

5'-TAATGAATTCTCAATTGATGGGAATAAAATAAG-3' (SEQ ID NO: 26) introducing an *Eco*RI site (3' primer)

On page 16, beginning at line 27, please amend the specification as follows (Please note that the text "GGTGGCTCCGGTGGT" has not been added by way of this amendment. This text was underlined in the specification as filed and it should be underlined in the unmarked version of this paragraph.):

The transmembrane (TM) and cytoplasmic (C) domains of hCD8 were amplified using the 3' primer described above and the following 5' primer:

5'-CATAGGCAACGGAGCCCAGATTTATGTAATTGGTGGCTCCGGTGGTGTCGACT TCGCCTGTGATATCTACATC-3' (SEQ ID NO: 27)

On page 17, beginning at line 1, please amend the specification as follows:

This amplified from position 532 and included a 15 base segment encoding a flexible GGSGG (SEQ ID NO: 35) amino acid linker (underlined), along with a unique *Sal*I site (highlighted). The resulting fragment was sub cloned into *Hind*III/*Sal*I digested pBluescript and called pBluescript-hCD8.

REMARKS

Applicants have carefully studied the Office Action mailed on July 28, 2003, which issued in connection with the above-identified application. The specification has been amended to include the proper identification of all amino acid and nucleotide sequences with sequence identifier numbers (SEQ ID NOS: 1-35). No new matter has been added by way of these amendments.

SUBSTITUTE SEQUENCE LISTING

A Substitute Sequence Listing is being submitted herewith. SEQ ID NO: 34 of the Substitute Sequence Listing is the full-length nucleotide sequence for cattle (bovine) CTLA-4. The cattle CTLA-4 sequence is shown in Figure 3. Nucleotides 296-355 of SEQ ID NO: 34 were accidentally omitted from Figure 3 as filed. A corrected replacement Figure 3 with the full-length cattle CTLA-4 sequence is in preparation and will be submitted in a subsequent submission to the USPTO.

No new matter has been added by way of the Substitute Sequence Listing and, specifically, by way of SEQ ID NO: 34. The specification supports full-length cattle CTLA-4 (SEQ ID NO: 34). In particular, SEQ ID NO: 34 is disclosed in reference 21 cited in the specification (Parsons et al. Immunogenetics 43(6), 388-391 (1996)). A copy of the National

Center for Biotechnology Information printout showing that the Parsons et al. reference discloses SEQ ID NO: 34 is attached at Tab 1.[1]

STATEMENT PURSUANT TO 37 C.F.R. 1.821(f)

Enclosed herewith is a paper copy and computer readable form (diskette) containing sequence disclosures. Pursuant to 37 C.F.R. § 1.821(f), Applicants hereby confirm that the contents of the paper copy of the substitute Sequence Listing filed herewith and entitled "SEQUENCE LISTING", and of the identically labeled diskette enclosed herewith, specifically the ASCII-encoded file therein labeled "Seqlist.txt", are identical. This sequence submission contains no new matter.

Consideration of the enclosed diskette and paper copy of a Substitute Sequence listing, are respectfully requested.

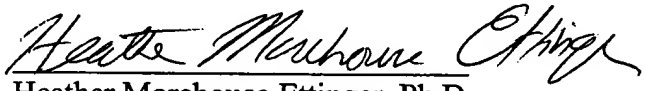
[1] In addition, SEQ ID NO: 34 was disclosed in and thus, has support in the priority application for the present application (GB 9809280.2)

CONCLUSION

Applicants request entry of the foregoing amendments and remarks in the file history of this application. In view of the above amendments and remarks, it is respectfully requested that the application be examined on its merits and that all pending claims be allowed and the case passed to issue.

Respectfully submitted,

Dated: October 28, 2003



Heather Morehouse Ettinger, Ph.D.
Reg. No. 51,658
Agent for Applicants

DARBY & DARBY P.C.
805 Third Avenue
New York, New York 10022
212-527-7700

☐ 1: X93305. B.taurus mRNA for...[gi:1369935] Links

```
LOCUS       BTCTLA4PT                666 bp    mRNA    linear   MAM 04-JUN-1996
DEFINITION  B.taurus mRNA for CTLA-4 protein.
ACCESSION   X93305
VERSION     X93305.1  GI:1369935
KEYWORDS    CTLA-4 gene; CTLA-4 protein.
SOURCE      Bos taurus (cow)
  ORGANISM  Bos taurus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
            Bovidae; Bovinae; Bos.
REFERENCE   1
  AUTHORS   Parsons,K.R., Young,J.R., Collins,B.A. and Howard,C.J.
  TITLE     Cattle CTLA-4, CD28 and chicken CD28 bind CD86: MYPPPY is not
            conserved in cattle CD28
  JOURNAL   Immunogenetics 43 (6), 388-391 (1996)
  MEDLINE   96186531
   PUBMED   8606060
REFERENCE   2  (bases 1 to 666)
  AUTHORS   Parsons,K.R.
  TITLE     Direct Submission
  JOURNAL   Submitted (21-NOV-1995) K.R. Parsons, Institute for Animal Health,
            Division of Immunology and Pathology, Compton, Newbury, Berkshire,
            RG20 7NN, UK
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      121 cctccagtgg tgctggctag cagccggggt gttgccagct tctcatgtga atatgagtct
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      421 atcggcaatg gaacccagat ttacgtcatt gatccagaac catgcccgga ttctgatttt
      481 ctcctctgga tcctggcagc agttagttca gggttgtttt tctacagctt cctcatcaca
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Oct 20 2003 14:38:52

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Dorling, Anthony

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<140> US 09/674,462
<141> 2001-05-08

<150> PCT/GB99/01350
<151> 1999-04-30

<150> GB-9809280.2
<151> 1998-04-30

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<170> PatentIn Ver. 2.1

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Ser Arg Thr Trp Pro Cys Thr Ala Leu Phe Ser Leu Leu Phe Ile Pro
            20                  25                  30

Val Phe Ser Lys Gly Met His Val Ala Gln Pro Ala Val Val Leu Ala
        35                  40                  45

Asn Ser Arg Gly Val Ala Ser Phe Val Cys Glu Tyr Gly Ser Ala Gly
    50                  55                  60

Lys Ala Ala Glu Val Arg Val Thr Val Leu Arg Arg Ala Gly Ser Gln
65                  70                  75                  80

Met Thr Glu Val Cys Ala Ala Thr Tyr Thr Val Glu Asp Glu Leu Thr
                85                  90                  95

Phe Leu Asp Asp Ser Thr Cys Thr Gly Thr Ser Thr Glu Asn Lys Val
            100                 105                 110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Val Asp Thr Gly Leu Tyr Ile
        115                 120                 125

Cys Lys Val Glu Leu Leu Tyr Pro Pro Pro Tyr Tyr Val Gly Met Gly
    130                 135                 140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
145                 150                 155                 160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe
                165                 170                 175

Tyr Ser Phe Leu Ile Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys
            180                 185                 190
```

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Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu
        195                 200                 205

Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
    210                 215                 220
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<400> 2

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<210> 3
<211> 400
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:pCTLA4-Ig construct (Figure 4)

<400> 3

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Met Ala Cys Ser Gly Phe Arg Ser His Gly Ala Trp Leu Glu Leu Thr
  1               5                  10                  15

Ser Arg Thr Trp Pro Cys Thr Ala Leu Phe Ser Leu Leu Phe Ile Pro
            20                  25                  30

Val Phe Ser Lys Gly Met His Val Ala Gln Pro Ala Val Val Leu Ala
        35                  40                  45

Asn Ser Arg Gly Val Ala Ser Phe Val Cys Glu Tyr Gly Ser Ala Gly
    50                  55                  60

Lys Ala Ala Glu Val Arg Val Thr Val Leu Arg Arg Ala Gly Ser Gln
65                  70                  75                  80

Met Thr Glu Val Cys Ala Ala Thr Tyr Thr Val Glu Asp Glu Leu Thr
                85                  90                  95

Phe Leu Asp Asp Ser Thr Cys Thr Gly Thr Ser Thr Glu Asn Lys Val
            100                 105                 110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Val Asp Thr Gly Leu Tyr Ile
        115                 120                 125

Cys Lys Val Glu Leu Leu Tyr Pro Pro Pro Tyr Tyr Val Gly Met Gly
    130                 135                 140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
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145 150 155 160

Asp Gly Gly Ser Gly Gly Ala Ala Glu Pro Lys Ser Cys Asp Lys Thr
165 170 175

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
180 185 190

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
195 200 205

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
210 215 220

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
225 230 235 240

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
245 250 255

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
260 265 270

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
275 280 285

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
290 295 300

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
305 310 315 320

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
325 330 335

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
340 345 350

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
355 360 365

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
370 375 380

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
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<212> DNA
<213> Artificial Sequence

<220>
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ctccagggaa ggggctggag tgggtctcag ctattcgtgg tagtggtggt agcacatact 180
acgcagactc cgtgaagggc cggttcacca tctccagaga caattccaag aacacgctgt 240
atctgcaaat gaacagcctg agagccgagg acacggccgt gtattactgt gcaagagctg 300
gtcgtatttt gtttgactat tggggccaag gtaccctggt caccgtctcg agtggtggag 360
gcggttcagg cggaggtggc tctggcggta gtgcacttca gtctgtgctg actcagccac 420

cctcagcgtc tgggaccccc gggcagcggg tcaccatctc ttgttctgga agcagctcca 480
acatcggaag taattatgta tactggtacc agcagctccc aggaacggcc cccaaactcc 540
tcatctatag gaataatcag cggccctcag gggtccctga ccgattctct ggctccaagt 600
ctggcacctc agcctccctg gccatcagtg ggctccggtc cgaggatgag gctgattatt 660
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<210> 5
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> Phage library

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Gly Arg Ile Leu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Ser Ala Leu Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly
130 135 140

Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn
145 150 155 160

Ile Gly Ser Asn Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala
165 170 175

Pro Lys Leu Leu Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro
180 185 190

Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile
195 200 205

Ser Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp
210 215 220

Asp Asp Ser Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
225 230 235 240

<210> 6

<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> Phage library

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gctgtatctg caaatgaaca gcctgagagc cgaggacacg gccgtgtatt actgtgcaag 300
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cctaggtgc 729

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<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> Phage library

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ccggcagccc ccagggaagg gactggagtg gattgggtat atctattaca gtgggagcac 180
caactacaac ccctccctca agagtcgagt caccatatca gtagacacgt ccaagaacca 240
gttctccctg aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcaag 300
aatgcggaag gataagtttg actattgggg ccaaggtacc ctggtcaccg tctcgagtgg 360
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caagtctggc acctcagcct ccctggccat cagtgggctc cggtccgagg atgaggctga 660
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<211> 739
<212> DNA
<213> Artificial Sequence

<220>
<223> Phage library

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taggagacag cctcagaagc tattatgcaa gctggtacca gcagaagcca ggacaggccc 540
ctgtacttgt catctatggt aaaaacaacc ggccctcagg gatcccagac cgattctctg 600
gctccagctc aggaaacaca gcttccttga ccatcactgg ggctcaggcg gaagatgagg 660
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<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<223> Phage library

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caaacgtgc 729

<210> 10
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> Phage library

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
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Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Gly Arg Ile Leu Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

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Gly Ser Ala Leu Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly
    130                 135                 140

Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn
145                 150                 155                 160

Ile Gly Ser Asn Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala
                165                 170                 175

Pro Lys Leu Leu Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro
            180                 185                 190

Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile
        195                 200                 205

Ser Gly Leu Arg Ser Glu Asp Glu Ala Ser Tyr Tyr Cys Ala Ala Trp
    210                 215                 220

Asp Asp Ser Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
225                 230                 235                 240


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<212> PRT
<213> Artificial Sequence

<220>
<223> Phage library

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Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Val Ser
            20                  25                  30

Ser Gly Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly
        35                  40                  45

Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn
    50                  55                  60

Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Met Arg Lys Asp Lys Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Ser Ala Leu Gln Ser Val Leu Thr Gln Pro Pro Ser
    130                 135                 140

Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser
145                 150                 155                 160

Ser Ser Asn Ile Gly Ser Asn Tyr Val Tyr Trp Tyr Gln Gln Leu Pro
                165                 170                 175
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Gly Thr Ala Pro Lys Leu Leu Ile Tyr Arg Asn Asn Gln Arg Pro Ser
180 185 190

Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser
195 200 205

Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Val
210 215 220

Ala Ala Trp Asp Asp Ser Leu Phe Val Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Thr Val Leu Gly Ala Ala
245

<210> 12
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<223> Phage library

<400> 12
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Arg Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Ala Pro Tyr Val Asn Thr Leu Val Phe Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Ser Ala Leu Ser Ser Glu Leu Thr Gln Asp Pro Ala Val
130 135 140

Ser Val Ala Leu Gly Gln Thr Val Arg Ile Thr Cys Gln Gly Asp Ser
145 150 155 160

Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Val Leu Val Ile Tyr Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Ser Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile
195 200 205

Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg

210 215 220

Asp Ser Ser Gly Phe Thr Val Phe Gly Gly Gly Thr Lys Leu Thr Val
225 230 235 240

Leu Gly

<210> 13
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> Phage library

<400> 13
Gln Val Gln Leu Leu Gln Ser Ala Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Ser Leu Gly Gly Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Ser Ala Leu Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser
130 135 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly
145 150 155 160

Ile Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
165 170 175

Lys Leu Leu Val Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn
210 215 220

Ser Tyr Arg Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
225 230 235 240

<210> 14

<211> 742
<212> DNA
<213> Homo sapiens

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aagccatggc ttgccttgga tttcagcggc acaaggctca gctgaacctg gctaccagga 120
cctggccctg cactctcctg ttttttcttc tcttcatccc tgtcttctgc aaagcaatgc 180
acgtggccca gcctgctgtg gtactggcca gcagccgagg catcgccagc tttgtgtgtg 240
agtatgcatc tccaggcaaa gccactgagg tccgggtgac agtgcttcgg caggctgaca 300
gccaggtgac tgaagtctgt gcggcaacct acatgatggg gaatgagttg accttcctag 360
atgattccat ctgcacgggc acctccagtg gaaatcaagt gaacctcact atccaaggac 420
tgagggccat ggacacggga ctctacatct gcaaggtgga gctcatgtac ccaccgccat 480
actacctggg cataggcaac ggaacccaga tttatgtaat tgatccagaa ccgtgcccag 540
attctgactt cctcctctgg atccttgcag cagttagttc ggggttgttt ttttatagct 600
ttctcctcac agctgtttct ttgagcaaaa tgctaaagaa aagaagccct cttacaacag 660
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<210> 15
<211> 223
<212> PRT
<213> Homo sapiens

<400> 15
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1 5 10 15

Thr Arg Thr Trp Pro Cys Thr Leu Leu Phe Phe Leu Leu Phe Ile Pro
20 25 30

Val Phe Cys Lys Ala Met His Val Ala Gln Pro Ala Val Val Leu Ala
35 40 45

Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly
50 55 60

Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln
65 70 75 80

Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr
85 90 95

Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val
100 105 110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile
115 120 125

Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly
130 135 140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
145 150 155 160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe
165 170 175

Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys
180 185 190

Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu
195 200 205

Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
210 215 220

<210> 16
<211> 773
<212> DNA
<213> Homo sapiens

<400> 16
aagcttcgag ccaagcagcg tcctggggag cgcgtcatgg ccttaccagt gaccgccttg 60
ctcctgccgc tggccttgct gctccacgcc gccaggccga gccagttccg ggtgtcgccg 120
ctggatcgga cctggaacct gggcgagaca gtggagctga agtgccaggt gctgctgtcc 180
aacccgacgt cgggctgctc gtggctcttc cagccgcgcg gcgccgccgc cagtcccacc 240
ttcctcctat acctctccca aaacaagccc aaggcggccg aggggctgga cacccagcgg 300
ttctcgggca agaggttggg ggacaccttc gtcctcaccc tgagcgactt ccgccgagag 360
aacgagggct actatttctg ctcggccctg agcaactcca tcatgtactt cagccacttc 420
gtgccggtct tcctgccagc gaagcccacc acgacgccag cgccgcgacc accaacaccg 480
gcgcccacca tcgcgtcgca gcccctgtcc ctgcgcccag aggcgtgccg gccagcggcg 540
gggggcgcag tgcacacgag ggggctggac ttcgcctgtg atatctacat ctgggcgccc 600
ttggccggga cttgtggggt ccttctcctg tcactggtta tcaccttta ctgcaaccac 660
aggaaccgaa gacgtgtttg caaatgtccc cggcctgtgg tcaaatcggg agacaagccc 720
agcctttcgg cgagatacgt ctaaccctgt gcaacagcca ctacatgaat tcc 773

<210> 17
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 17
ttgaagctta gccatggctt gctctgga 28

<210> 18
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 18
taatgaattc tcaattgatg ggaataaaat aag 33

<210> 19
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 19
cggttctgca gcaccaccgg agccaccatc agaatctggg catggttctg gatcaatgac 60

<210> 20
<211> 25

<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 20
gagctgaaac gggcggccgc agaac 25

<210> 21
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 21
ctggcctgca gcattcagat cc 22

<210> 22
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 22
ttcaaagctt caggatcctg aaaggttttg 30

<210> 23
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 23
taatgaattc tcaattgatg ggaataaaat aag 33

<210> 24
<211> 76
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 24
gatgtagata tcacaggcga agtcgacacc accggagcca ccaattacat aaatctgggc 60
tccgttgcct atgccc 76

<210> 25
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 25
tcgcgcccaa gcttcgagcc aagcagcgt 29

<210> 26
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 26
taatgaattc tcaattgatg ggaataaaat aag 33

<210> 27
<211> 73
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: primer

<400> 27
cataggcaac ggagcccaga tttatgtaat tggtggctcc ggtggtgtcg acttcgcctg 60
tgatatctac atc 73

<210> 28
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: linker

<400> 28
Gly Gly Ser Gly Gly Ala Ala
1 5

<210> 29
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: hexapeptide motif

<400> 29
Met Tyr Pro Pro Pro Tyr
1 5

<210> 30
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: hexapeptide motif

<400> 30
Leu Tyr Pro Pro Pro Tyr
1 5

<210> 31
<211> 223
<212> PRT
<213> Homo sapiens

<400> 31
Met Ala Cys Leu Gly Phe Gln Arg His Lys Ala Gln Leu Asn Leu Ala
1 5 10 15

Ala Arg Thr Trp Pro Cys Thr Leu Leu Phe Phe Leu Leu Phe Ile Pro
20 25 30

Val Phe Cys Lys Ala Met His Val Ala Gln Pro Ala Val Val Leu Ala
35 40 45

Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly
50 55 60

Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln
65 70 75 80

Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr
85 90 95

Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val
100 105 110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile
115 120 125

Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly
130 135 140

Asn Gly Ala Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
145 150 155 160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe
165 170 175

Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys
180 185 190

Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu
195 200 205

Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
210 215 220

<210> 32
<211> 221
<212> PRT
<213> Bos taurus

<400> 32
Met Ala Cys Ser Gly Phe Gln Ser His Gly Thr Trp Trp Thr Ser Arg
1 5 10 15

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Thr Trp Pro Cys Thr Ala Leu Phe Phe Leu Val Phe Ile Pro Val Phe
            20                  25                  30

Ser Lys Gly Met Asn Val Thr Gln Pro Pro Val Val Leu Ala Ser Ser
        35                  40                  45

Arg Gly Val Ala Ser Phe Ser Cys Glu Tyr Glu Ser Ser Gly Lys Ala
    50                  55                  60

Asp Glu Val Arg Val Thr Val Leu Arg Glu Ala Gly Ser Gln Val Thr
65                  70                  75                  80

Glu Val Cys Ala Gly Thr Tyr Met Val Glu Asp Glu Leu Thr Phe Leu
                85                  90                  95

Asp Asp Ser Thr Cys Ile Gly Thr Ser Arg Gly Asn Lys Val Asn Leu
            100                 105                 110

Thr Ile Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Val Cys Lys
        115                 120                 125

Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Val Gly Ile Gly Asn Gly
    130                 135                 140

Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser Asp Phe
145                 150                 155                 160

Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe Tyr Ser
                165                 170                 175

Phe Leu Ile Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys Arg Ser
            180                 185                 190

Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu Pro Glu
        195                 200                 205

Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
    210                 215                 220
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<210> 33
<211> 672
<212> DNA
<213> Homo sapiens

<400> 33
atggcttgcc ttggatttca gcggcacaag gctcagctga acctggctgc caggacctgg 60
ccctgcactc tcctgttttt tcttctcttc atccctgtct tctgcaaagc aatgcacgtg 120
gcccagcctg ctgtggtact ggccagcagc cgaggcatcg ccagctttgt gtgtgagtat 180
gcatctccag gcaaagccac tgaggtccgg gtgacagtgc ttcggcaggc tgacagccag 240
gtgactgaag tctgtgcggc aacctacatg atggggaatg agttgacctt cctagatgat 300
tccatctgca ccggcacctc cagtggaaat caagtgaacc tcactatcca aggactgagg 360
gccatggaca cgggactcta catctgcaag gtggagctca tgtacccacc gccatactac 420
ctgggcatag gcaacggagc ccagatttat gtaattgatc cagaaccgtg cccagattct 480
gacttcctcc tctggatcct tgcagcagtt agttcggggt tgtttttta tagctttctc 540
ctcacagctg tttctttgag caaaatgcta aagaaaagaa gccctcttac aacaggggtc 600
tatgtgaaaa tgcccccaac agagccagaa tgtgaaaagc aatttcagcc ttattttatt 660
cccatcaatt ga 672

<210> 34
<211> 666
<212> DNA

<213> Bos taurus

<400> 34
atggcttgct ctggattcca gagtcatggg acttggtgga catctaggac ctggccctgc 60
actgccctat tttttcttgt cttcatccct gttttctcta aagggatgaa tgtgacccag 120
cctccagtgg tgctggctag cagccggggt gttgccagct tctcatgtga atatgagtct 180
tcaggcaaag ctgacgaggt ccgggtgaca gtgctgcggg aggcaggcag ccaggtgacc 240
gaagtctgtg ctgggaccta catggtggag gatgagctaa ccttcctgga tgattccact 300
tgcattggca cctccagagg aaacaaagtg aacctcacca tccaagggct gagggccatg 360
gacactgggc tctatgtctg caaagtggag ctcatgtacc cgccgcccta ctacgtgggc 420
atcggcaatg gaacccagat ttacgtcatt gatccagaac catgcccgga ttctgatttt 480
ctcctctgga tcctggcagc agttagttca gggttgtttt tctacagctt cctcatcaca 540
gctgtttctt tgagcaaaat gctaaagaaa agaagccctc ttactacagg ggtctatgtg 600
aaaatgcccc caacagagcc agaatgtgaa aagcaatttc agccttattt tattcccatc 660
aattga 666

<210> 35
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: linker

<400> 35
Gly Gly Ser Gly Gly
1 5